REMARKS

After entry of the above amendments, Claims 46, 49-53, 81, 186, 194-199, 217-220, 246, 272-273 and 280-299 will be pending.

A. Section 112 Rejections

1. Indefiniteness Rejections

The Examiner has rejected Claims 46, 49-53, 81, 186, 194-199, 217-220, 246, 272-273 and 280-299 on the basis that they are indefinite.

It is the Examiner's position that Claims 46, 81, 186 and 272 and claims dependent on them are indefinite for the use of the expression "10% dephosphorylated". What is meant by 10% and other levels of dephosphorylation is defined on page 7, lines 11-20, of the specification. Also see page 8, lines 10-19, of the specification for a description of how to determine levels of phosphorylation and dephosphorylation. Clearly, dephosphorylation of any phosphorylated amino acid (Ser, Thr and Tyr) is intended. For further confirmation of this, see page 7, line 21 through page 8, line 10 of the specification.

It is the Examiner's position that Claims 281, 287-288 and 294 are indefinite for the use of the expression "fragment that is unphosphorylated". An "unphosphorylated" protein or fragment thereof means that it is not phosphorylated at all. See page 6, line 10 through page 7, line 10, of the specification. For instance, Claim 281 refers back to Claim 46, and Claim 46 recites "at least 10% dephosphorylated" which can, of course, include 100% dephosphorylated (*i.e.*, unphosphorylated). The phrase "fragment that is unphosphorylated" does not mean a partially phosphorylated fragment which is not further phosphorylated, as suggested by the Examiner, and it is submitted that no basis for assigning such a meaning to the phrase can be found in the present application.

The Examiner continues to reject Claims 272 and 273 as indefinite for the use of the expression "attached to." As noted in Applicant's previous response, "attached to" in Claim 272

means covalent binding (see page 15, lines 21-22, and page 17, lines 16-19). Accordingly, Claim 272 has been amended to specify covalent attachment.

2. Written Description Rejection

The Examiner has rejected Claims 46, 49-53, 81, 186, 194-199, 217-220, 246 and 280-299 on the basis that they contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors had possession of the claimed invention at the time of the filing of the application. In particular, the Examiner is concerned with the reference in the claims to "fragments" of phosvitin. Applicant respectfully traverses this rejection.

First, it should be noted that the expression "phosvitin or a fragment thereof" was contained in the specification and claims of the application as filed (see, *e.g.*, page 8, lines 20-21, of the specification and original Claim 2). There is a strong presumption that an adequate written description of the claimed invention is present when the application is filed. MPEP § 2163.

Second, it is submitted that those skilled in the art would readily understand what was meant by phosvitin fragments and know how to make them. It is not necessary to disclose in detail what is conventional or well known to one of ordinary skill in the art. MPEP § 2163.

For instance, those skilled in the art would have known that phosvitin fragments could be made by proteolytic degradation of phosvitin. See, *e.g.*, Jiang et al., *J. Agric. Food Chem.*, **48:**990-994 (2000), Goulas et al., *J. Protein Chem.*, **15(1)**:1-9 (1996) (copy enclosed) and Khan et al., *J. Agric. Food Chem.*, **46**:4977-4981 (1998). In particular, Jiang et al. (cited in the present application at page 7, lines 21-25, page 8, lines 7-9 and Example 2) describes a large variety of dephosphorylated phosvitin fragments and how to make them.

The Examiner contends that phosvitin was known to be resistant to fragmentation by proteolysis. However, the patent cited by the Examiner in support of this proposition teaches the opposite. See U.S. Patent No. 5,665,868, column 4, lines 32-37, and Example 9. Even assuming that such a problem existed at some point, it had been overcome, at least for the preparation of

dephosphorylated phosvitin fragments, which are the type of fragments used in the present invention. See, *e.g.*, Jiang et al., *J. Agric. Food Chem.*, **48:**990-994 (2000).[1]

Of course, those skilled in the art would also have known that phosvitin fragments (*i.e.*, phosvitin peptides) useful in the practice of the present invention could be made by peptide synthetic methods or recombinant DNA methods, as described in the present specification. See, *e.g*, page 6, lines 2-6, page 6, lines 11-19, and page 7, lines 1-7, of the specification. Also see U.S. Patent No. 5,665,868 (cited by the Examiner), column 1, lines 37-43.

It is the Examiner's position that the specification fails to teach the correlation of the fragment structure with the pharmaceutical function thereof. However, this is incorrect. The specification teaches that any compound used in the practice of the invention, including of course phosvitin fragments, must include at least one unphosphorylated phosphorylation site. See, *e.g.*, page 5, lines 25-26, page 6, lines 10-11, and page 13, line 7. Thus, the Examiner's hypothesis that the expression "phosvitin fragment" includes peptides without a phosphorylation site is incorrect.

For all of the above reasons, Applicant submits that the written description conveys to those skilled in the art that Applicant had possession of the claimed invention as of the filing of the application, and this rejection should be withdrawn.

3. Lack of Enablement Rejections

First, the Examiner has rejected Claims 49-53, 81, 186, 194-199, 217-220, 246 and 280-299 on the basis that the specification does not provide enablement for pharmaceutical compositions comprising phosvitin fragments. Applicant traverses this rejection for the reasons given in the previous section.

Second, the Examiner has also rejected Claims 49-53, 81, 186, 194-199, 217-220, 246 and 280-299 on the basis that the specification does not provide enablement for pharmaceutical

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[1] The Xu et al. article cited by the Examiner confirms the teachings of Jiang et al., but it is not prior art and is, therefore, irrelevant to the present discussion.

compositions comprising phosvitin which is dephosphorylated more than 40%. Applicant respectfully traverses this rejection.

In particular, Applicant teaches that the preferred method of dephosphorylation is described in Jiang et al., *J. Agric. Food Chem.*, **48:**990-994 (2000). See page 7, line 21 through page 8, line 9, of the specification. This article teaches that phosvitin can be desphosphorylated up to about 96%. See page 992, section entitled "Alkaline Dephosphorylation of Phosvitin".[2] Other references teach 100% dephosphorylation of phosvitin. See, *e.g.*, Kato et al., *Agric. Biol. Chem.*, **51(11)**, 2989-2994 (1987)[3], page 2991, column 2, lines 8-9 of the text. Further, as noted above, phosvitin and phosvitin fragments could be produced by synthetic chemical methods or recombinant DNA methods to produce unphosphorylated (*i.e.*, 100% dephosphorylated) proteins and peptides.

For all the foregoing reasons, the Examiner is asked to withdraw these rejections.

D. Section 103 Rejections

1. Rejection of Claims 46, 49-51, 81, 186, 194-197, 219-220, 246, 280, 282-284, 289-291, 295 and 297-299

The Examiner has rejected Claims 46, 49-51, 81, 186, 194-197, 219-220, 246, 280, 282-284, 289-291, 295 and 297-299 as unpatentable over U.S. Patent No. 5,279,814 (Wuelknitz et al.)

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[2] Jiang et al. also teaches that a specific degree of dephosphorylation of phosvitin and phosvitin fragments can be achieved by adjusting the dephosphorylation conditions. See Jiang et al., page 992, sections entitled "Alkaline Dephosphorylation of Phosvitin" (including Figure 2) and "Tryptic Digests of Alkaline Dephosphorylated Phosvitin".

[3] This is the reference cited by the Examiner in support of the proposition that the maximum amount of dephosphorylation of phosvitin taught by the prior art was 40%. However, 40% was the maximum amount of dephosphorylation obtained using a particular phosphatase. See Table II, page 2991. Complete dephosphorylation was obtained using alkaline treatment. See page 2991, column 2, lines 8-9 of the text. Thus, the reference relied on by the Examiner actually teaches the opposite of the Examiner's position.

in view of Jiang et al., *J. Agric. Food Chem.*, **48:**990-994 (2000) (Jiang). Applicant respectfully traverses this rejection.

First, Wuelknitz et al. is not a proper reference against these claims. Wuelknitz et al. teaches oral and dental compositions. In the restriction requirement dated March 27, 2006, the Examiner required restriction between the pharmaceutical compositions of the presently rejected claims and claims directed to oral care compositions. In doing so, the Examiner took the position that the pharmaceutical compositions of the rejected claims are patentably distinct (*i.e.,* not obvious) from oral care compositions, such as those taught by Wuelknitz et al. (see the three paragraphs discussing inventions 3, 6, 7, 8 and 9 on pages 3-4 of the restriction requirement). Accordingly, Wuelknitz et al. is not a proper reference against the rejected claims, and this rejection should be withdrawn for this reason alone.

Second, even assuming that Wuelknitz et al. is a proper reference, the combined teachings of Wuelknitz et al. and Jiang would not have made the rejected claims obvious.

Wuelknitz et al. teaches oral and dental compositions comprising phosvitin. The phosvitin, in combination with fluoride, is used to protect the teeth against demineralization of the enamel. As correctly noted by the Examiner, the phosvitin used in the Wuelknitz et al. compositions is phosvitin as it is obtained from egg yolks without any dephosphorylation. Indeed, dephosphorylating phosvitin for use in the Wuelknitz et al. compositions would have been contrary to the teachings of Wuelknitz et al. that phosphorylation is necessary for the activity of phosvitin to protect teeth against demineralization of enamel. See column 1, lines 18-30 of Wuelknitz et al.

Jiang teaches that dephosphorylated fragments of phosvitin can be used to solubilize calcium, remove calcium from insoluble phosphate precipitates and inhibit the formation of insoluble calcium phosphate. See section entitled "Formation of Soluble Complexes with Calcium", pages 993-994 of Jiang. However, the primary constituent of tooth enamel is hydroxyapatite (see Wuelknitz et al., column 1, lines 26-30), and hydroxyapatite has the formula

$Ca_{10}(PO_4)_6(OH)_2$. Solubilizing calcium, removing it from insoluble calcium phosphate precipitates and inhibiting the formation of insoluble calcium phosphate would, therefore, be detrimental to tooth enamel and could result in its demineralization. Protecting against demineralization is the goal of Wuelknitz et al., so those skilled in the art would have not used the peptides of Jiang in the oral and dental compositions of Wuelknitz et al.

For all of the above reasons, the combined teachings of Wuelknitz et al. and Jiang would not have made the rejected claims obvious, and this rejection should be withdrawn.

2. Rejection of Claims 218 and 296

The Examiner has rejected Claims 218 and 296 as unpatentable over U.S. Patent No. 5,279,814 (Wuelknitz et al.) in view of Jiang et al., *J. Agric. Food Chem.*, **48**:990-994 (2000) (Jiang) and further in view of U.S. Patent No. 6,503,483 (Shuch et al.).

Applicant respectfully traverses this rejection for the reasons given in the previous section and for the following additional reasons.

Shuch et al. teaches oral care compositions and other oral care products. Accordingly, Shuch et al., like Wuelknitz et al., is an improper reference against the rejected claims for the reasons discussed in the previous section. Further, Shuch et al. teaches nothing about phosvitin.

For all of the above reasons, the combined teachings of Wuelknitz et al., Jiang and Shuch et al. would not have made the rejected claims obvious, and this rejection should be withdrawn.

CONCLUSION

Applicant believes that all pending claims are in condition for allowance and such disposition is respectfully requested. In the event that a telephone conversation would further prosecution and/or expedite allowance, the Examiner is invited to contact the undersigned.

Respectfully submitted,

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